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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/289,576	04/09/1999	RICHARD C. ALLEN	398802000600	8803

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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/289,576	ALLEN ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-12,17 and 19-36* is/are pending in the application.

4a) Of the above claim(s) *19-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 7, 2004 (hereinafter referred to as "the response") has been entered. Claim 1 has been amended. Claims 13-16 have been cancelled.

Claims 1-6, 8-12, 17, and 19-36 remain pending in the instant application.

Claims 19-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in Paper No. 10.

Accordingly, Claims 1-6, 8-12, and 17 are examined herein.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 7, 2004 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-12, and 17 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 2-6 of the Office Action mailed 5/7/01, on pages 2-6 of the Office Action mailed 2/27/02, on pages 3-6 of the Office Action mailed 11/18/02, and on pages 3-4 of the Office Action mailed 7/2/03, and for further reasons as discussed herein, as containing subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At page 8, paragraph 2 of the response, Applicants point out that the claims have been amended so that they are now directed to a method for providing dopamine or a dopamine precursor to a dopamine-deficient prefrontal cortex of a subject with schizophrenia. The claims have been amended so that the phrase "wherein said cell/support complex is administered in an amount effective to alleviate a negative symptom of schizophrenia. Nevertheless, the specification clearly asserts that the utility of the invention is to alleviate a symptom of schizophrenia. Enablement is evaluated in view of the asserted utility. While the claims no longer specifically recite alleviating a symptom of schizophrenia, the specification must enable the claimed invention. In the instant case, since the asserted utility is for treatment of schizophrenia, the specification must enable amelioration of a symptom of schizophrenia. In the absence of a therapeutic effect, the claimed invention would lack utility. However, the asserted utility of alleviating a symptom of schizophrenia is accepted as a credible utility, albeit one that is not enabled by the instant specification.

At page 8, paragraph 3 of the response, Applicants argue that the specification provides all the necessary teachings to enable the invention. This argument is not persuasive because the specification does not provide the necessary teachings to enable one of skill in the art to produce a therapeutic effect without undue experimentation. The claims are very broad in scope, covering the use of any cell type, as well as wide variety of combinations of cell type and support matrix. The cells may be unmodified or genetically modified, using any genetic modification that would aid in the production of dopamine or a dopamine precursor. Thus, the claims cover a very large number of possible combinations of these various parameters. However, it is left up to the skilled artisan to come up with a combination that produces a therapeutic effect upon delivery to the prefrontal cortex of a subject with schizophrenia. Given the unpredictability in the art, such a task would clearly require undue experimentation.

At page 9 of the response, Applicants argue that the current state of the art supports the association of the negative symptoms of schizophrenia with regional dopamine deficits in the brain. Applicants point to the reference of Abi-Dargham (2003). Of note, the reference points out that the putative role of dopamine systems in the pathophysiology and treatment of schizophrenia has been the subject of intense research efforts over the past 50 years (page 404, column 1, paragraph 1). Moreover, as discussed in the previous Office Action (page 3, paragraph 2 of the Office Action mailed 7/2/03), while increasing dopamine levels within the prefrontal cortex may be desirable, the instant specification does not teach how to generate dopamine levels that are sufficient to reduce a symptom of schizophrenia. It is a huge leap to go from a suggestion to increase dopamine activity in the prefrontal cortex as a treatment for schizophrenic patients to actually providing an enabled protocol for achieving the desired treatment. At present, the effect of dopamine replenishment within the prefrontal cortex of a diseased brain is unknown. Thus, one of skill in the art would look to the instant specification to provide these teachings. However, the instant specification does not adequately teach a protocol, as claimed, that could be used to effect the required level of dopamine replenishment.

At page 9, paragraph 2 of the response, Applicants assert that a well-understood etiology of schizophrenia is not required for enablement of the claimed invention. This is not persuasive because the state of the art is an important factor in evaluating enablement. In the instant case, the state of the art for schizophrenia, cell therapy, and *ex vivo* gene therapy are all highly unpredictable, for reasons of record. The complexity of the nervous system poses a formidable challenge for cell therapy approaches to treating disorders of the central nervous system. For schizophrenia, the factors underlying the pathology within the prefrontal cortex are presently unknown. Thus, the effect of cell therapy protocols that provide dopamine to a localized region of the brain is unpredictable given the limited information available in the prior art and the instant specification. Even for those diseases where the etiology is understood quite well, development of cell therapy protocols has been an enormous challenge. For example, although the

etiology of diabetes is well understood, intensive effort has been applied to devising cell therapy protocols for the treatment of diabetes with very limited success.

Given the lack of applicable working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to the wide variety of cell types that could be used, and the unpredictability for achieving a therapeutic effect upon the transplantation of a cell/support complex, undue experimentation would have been required for one skilled in the art to practice the claimed method of the invention in a human patient for therapeutic benefit.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite in its recitation of "the negative symptom" because the phrase lacks antecedent basis.

Conclusion

No claims are allowed.

This application contains claims 19-36 drawn to an invention nonelected without traverse in Paper No. 10. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114.

Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to William Phillips, whose telephone number is (571) 272-0548.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER